J = 7.1 Hz, 3 H), 0.61 (t, J = 7.2 Hz, 3 H); mass spectrum, m/e 450 (M^+, ^{80}Se), 448 (M^+, ^{78}Se). Anal. Calcd for $C_{23}H_{30}O_2SSe$: C, 61.45; H, 6.73; S, 7.13. Found: C, 61.14; H, 6.87; S, 6.84.

6-(*p*-Tolylsulfonyl)-4,5-decadiene (14). Selenide **12** (225 mg, 0.50 mmol) and MCPBA (94 mg, 0.55 mmol) were refluxed 2.5 h in 10 mL of chloroform. The solution was then concentrated and preparative TLC (hexane–ethyl acetate, 4:1; R_f 0.59) furnished 140 mg (96%) of allene **14**: bp (bulb-to-bulb) 150–160 °C (0.25 mm); IR (film) 1946, 1592, 1304, 1153 cm^{-1}; NMR (200 MHz) 7.75 (d, J = 7.7 Hz, 2 H), 7.31 (d, J = 7.7 Hz, 2 H), 5.76 (m, 1 H), 2.43 (s, 3 H), 2.26 (m, 2 H), 2.07 (m, 2 H), 1.5–1.2 (complex, 6 H), 0.92 (t, J = 7.6 Hz, 3 H), 0.84 (t, J = 7.5 Hz, 3 H); mass spectrum, m/e 292 (M^+, faint). Anal. Calcd for $C_{17}H_{24}O_2S$: C, 69.82; H, 8.27; S, 10.97. Found: C, 69.62; H, 8.27; S, 10.75.

1,1-Bis(phenylseleno)-2-(*p*-tolylsulfonyl)propene (16). Selenosulfonate **1** (311 mg, 1.00 mmol), 1-(trimethylsilyl)propyne (112 mg, 1.00 mmol) and AIBN (8 mg, 0.05 mmol) were dissolved in 0.5 mL of benzene in a sealed glass tube and heated for 4 days at an oil-bath temperature of 120 °C. The contents were then separated by preparative TLC (hexane–ethyl acetate, 4:1; R_f 0.24) to furnish 227 mg (90%) of **16**: mp 122.5–123.5 °C (from ether–hexane); IR (KBr) 1592, 1572, 1303, 1152, 830, 817 cm^{-1}; NMR (60 MHz) 7.86 (d, J = 8 Hz, 2 H), 7.4–6.75 (complex, 12 H), 2.31 (s, 3 H), 2.23 (s, 3 H); mass spectrum, m/e 508, 506, and 504 (M^+ of $^{80}Se_2$, ^{80}Se–^{78}Se, and $^{78}Se_2$, respectively). Anal. Calcd for $C_{22}H_{20}O_2SSe_2$: C, 52.18; H, 3.98; S, 6.33. Found: C, 52.38; H, 3.90; S, 6.36.

Deselenization of Ketene Diselenoacetal 16. The title compound **16** (128 mg, 0.25 mmol) was dissolved in 20 mL of methanol–THF (3:1), and the solution was added to $NiCl_2{\cdot}6H_2O$ (684 mg, 2.5 mmol) in 5 mL of methanol. Sodium borohydride (284 mg, 7.5 mmol) was then added in portions with continuous stirring. The reaction mixture was filtered through Celite, concentrated, and separated by preparative TLC (hexane–ethyl acetate, 4:1; R_f 0.16) to afford 27 mg (54%) of isopropyl *p*-tolyl sulfone [mp 76–79 °C (lit.[18] mp 80 °C)], identified by its IR and NMR spectra.

Registry No. **1**, 68819-94-3; (*E*)-**2**, 86410-04-0; (*E*)-**3**, 86409-90-7; (*E*)-**4**, 87517-76-8; (*E*)-**6**, 87517-77-9; (*E*)-**6-*d***, 87517-84-8; (*E*)-**10**, 87517-78-0; (*E*)-**11**, 87517-79-1; (*E*)-**12**, 87517-80-4; (*E*)-**13**, 87517-81-5; **14**, 87517-82-6; **16**, 87517-83-7; 1-phenyl-1-hexyne, 1129-65-3; 5-decyne, 1942-46-7; 1-(trimethylsilyl)propyne, 6224-91-5; isopropyl *p*-tolyl sulfone, 51751-71-4.

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Deacylation and Deformylation of Pyrroles

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Introduction

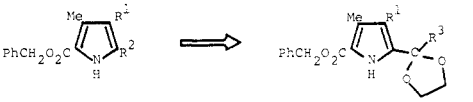
Unsubstituted positions on pyrrole rings tend to be reactive and hence often require protection during synthetic sequences.[1] Such positions in monopyrroles and porphyrins are usually protected with halogen atoms that can be removed, with variable success,[2] using catalytic hydrogenation. We recently communicated[3] that 3-acetylpyrroles and acetylporphyrins can be deacetylated by heating with ethanedithiol/BF_3 in acetic acid, and thus exploited the acetyl group as a porphyrin protecting group

Scheme I. Deacetylation, Deformylation, and Acetal Formation with Pyrroles Using Ethanedithiol and Boron Trifluoride

	R^1	R^2	R^3	R^4		R^1	R^2	R^3	R^4	Yield
1	$PhCH_2$	Me	COMe	Me	5	$PhCH_2$	Me	H	Me	(95%)
2	$PhCH_2$	H	COMe	Me	6	$PhCH_2$	H	H	Me	(55%)
3	Et	Me	CHO	Me	7	Et	Me	H	Me	(45%)
4	$PhCH_2$	Me	CO_2Me	CHO	8	$PhCH_2$	Me	CO_2Me		(64%)

Scheme II. Deacetylation, Deformylation, and Acetal/Ketal Formation with Pyrroles Using Ethylene Glycol and *p*-Toluenesulfonic Acid

	R^1	R^2	R^3		R^1	R^2	Yield
1	$PhCH_2$	Me	COMe	5	$PhCH_2$	Me	(95%)
3	Et	Me	CHO	7	Et	Me	(83%)
10	Et	CH_2CO_2Et	CHO	11	Et	CH_2CO_2Et	(35%)



	R^1	R^2		R^1	R^3	Yield
12	Me	COMe	13	Me	Me	(84%)
14	$CH_2CH_2CO_2Me$	CHO	17	$CH_2CH_2CO_2Me$	H	(86%)
15	Et	CHO	18	Et	H	(80%)
16	CO_2Me	CHO	19	CO_2Me	H	(96%)

in a partial synthesis of dehydrocoproporphyrin (S-411 porphyrin).[4] In this paper we give full details of the deacylation process in pyrrole systems, modify it so that less obnoxious reagents are used, and extend the method to deformylation. The process of deacetylation is important in pyrrole synthetic chemistry since acetylpyrroles are readily available via standard ring fabrication routes,[5,6] but unsubstituted pyrroles, in contrast, are not nearly so accessible.

Scheme I shows the results of attempts to deacetylate and deformylate pyrroles **1–4** with use of ethanedithiol and BF_3 in acetic acid, and a general method is given in the Experimental Section. The 3-acetylpyrroles **1** and **2** were efficiently transformed, under these conditions, into the corresponding 3-unsubstituted pyrroles **5** and **6**. Likewise, the 3-formylpyrrole **3** was deformylated in 45% yield to give pyrrole **7**. Attempts to deformylate the pyrrole **4** bearing three electron-withdrawing substituents were unsuccessful, and the corresponding acetal **8** was obtained in 64% yield.

Owing to the obnoxious nature of ethanedithiol, the deacetylations and deformylations were also attempted

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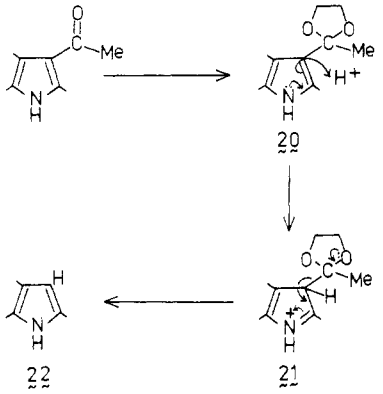
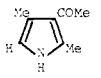
Scheme III. General Mechanism for Deacetylation of a 3-Acetylpyrrole



with ethylene glycol and neopentyl glycol, and these results are given in Scheme II. Pyrrole **1** was smoothly deacetylated with ethylene glycol and *p*-toluenesulfonic acid in toluene during 20 h to give a >90% yield of pyrrole **5**. When neopentyl glycol was used in place of the ethylene glycol, a 77% yield was obtained in only 2 h. Likewise, the *tert*-butyl ester corresponding to pyrrole **1** was deacetylated in 45% yield with ethylene glycol, showing that a *tert*-butyl ester can survive these conditions. In contrast, the 5-unsubstituted 3-acetylpyrrole **9** was recovered un-



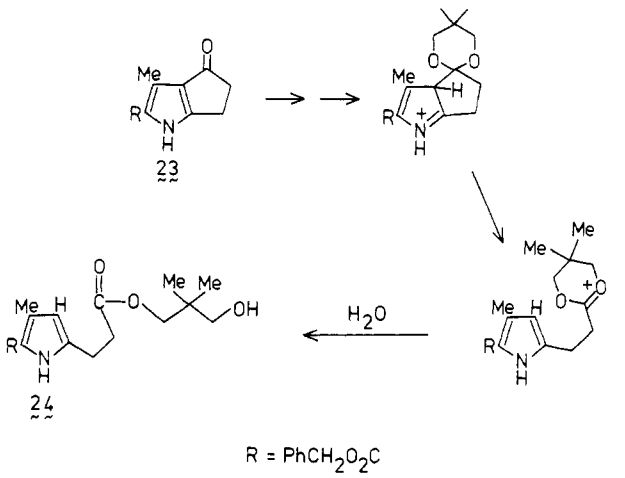
changed from the reaction mixture, and its lack of reactivity toward deacetylation may be due to protonation at the unsubstituted position during the reaction (see later). Though copper(II) 2,4-diacetyldeuteroporphyrin IX dimethyl ester was efficiently deacetylated with ethanedithiol,[3,4] it was recovered unchanged when attempts to deacetylate it with ethylene glycol were made.

Deformylation with ethylene glycol and *p*-toluenesulfonic acid was attempted with pyrroles **3** and **10** (Table II) and 83% and 35% yields of pyrroles **7** and **11**, respectively, were obtained.[7] Attempts to deacetylate the 2-acetylpyrrole **12** under similar conditions were unsuccessful, the corresponding ketal **13** being obtained in 84% yield. Likewise, attempts to deformylate the 2-formylpyrroles **14–16** resulted in formation of the corresponding acetals (**17–19**, respectively).

Scheme III shows a plausible mechanism for the deacetylation reaction. It involves initial ketal (**20**) formation (and we have checked that these ketals, produced separately under milder conditions, are efficiently deacetylated in the reaction), followed by electrophilic substitution (protonation) at the substituted carbon to give **21**. Presumably in order to regain its aromatic stability and concomitantly expell the bulky protected acetyl group, the fragment shown is then cleaved to give the unsubstituted pyrrole **22**.

In order to substantiate the mechanistic proposal in Scheme III, the pyrrole **23** was subjected to deacetylation conditions with use of neopentyl glycol and *p*-toluenesulfonic acid. The product obtained was fully characterized and identified as **24**, in which the expelled "acetyl" group is retained on the tail of the α-substituent. Isolation

Scheme IV. Partial Mechanism for Deacylation of Pyrrole 23



of the ester **24** confirms the gross mechanism (Scheme III) and is proposed to proceed as shown, in this particular case, in Scheme IV.

Experimental Section

Melting points were measured on a hot-stage apparatus and are uncorrected. Neutral alumina (Merck) was used for column chromatography, and preparative TLC was carried out on 20 × 20 cm glass plates coated with Merck GF 254 silica gel (1 mm thick). Analytical TLC was performed by using Merck silica gel 60 F 254 precoated sheets (0.2 mm). Proton NMR spectra were measured at 360 MHz by using a Nicolet NT-360 spectrometer or at 90 MHz with a Varian EM-390 spectrometer, in $CDCl_3$ solution with tetramethylsilane as internal standard. Mass spectra were measured (direct insertion probe, 70 eV, 50 μA, source temperature ca. 200 °C) with a Finnegan 3200 mass spectrometer. Elemental analyses were performed at the Berkeley Microanalytical Laboratory, University of California, Berkeley.

General Procedure for Deacylation or Deformylation Using Ethanedithiol. The 3-acetyl- or 3-formylpyrrole (200 mg) in acetic acid (15 mL) was treated with boron trifluoride etherate (distilled, 0.5 mL) and ethanedithiol (1.5 mL) and then heated under reflux for 1.5–4 h (monitoring by analytical TLC). The mixture was cooled, diluted with dichloromethane (50 mL), and washed with water (50 mL), 2 N sodium hydroxide (50 mL), and finally again with water (30 mL). The organic phase was dried (anhydrous Na_2SO_4) and evaporated to dryness to give a residue, which was chromatographed on thick-layer TLC plates (elution with 2% methanol in dichloromethane). The major (central) band was extracted from the silica with 5% methanol in dichloromethane, and the solvent was evaporated to give a residue. The upper band was usually nonpyrrolic and the lower band was starting material; occasionally a small amount of dithioketal or dithioacetal was also isolated from the plate. The residue from above was crystallized from dichloromethane/hexane.

General Procedure for Deacylation or Deformylation Using Ethylene Glycol. The 3-acetyl- or 3-formylpyrrole (2.5 g) in dry benzene (135 mL) was treated with *p*-toluenesulfonic acid hydrate (120 mg) and dry ethylene glycol (23 mL) and then heated at reflux under nitrogen for up to 20 h (with TLC monitoring). After addition of water (100 mL), the mixture was extracted with chloroform (2 × 100 mL), which was washed with saturated aqueous sodium bicarbonate (200 mL) and then water (200 mL). The organic phase was dried (anhydrous Na_2SO_4). In many cases the solvent could then be evaporated and the product crystallized directly, but on occasion it was necessary to submit the residue to column or preparative TLC purification.

Most compounds used and deacylated or deformylated are standard literature compounds.[1,5,6] Those compounds that are new were characterized on the basis of data given below.

Dithioacetal 8 from Benzyl 5-Formyl-4-(methoxycarbonyl)-3-methylpyrrole-2-carboxylate (4): mp 93–94 °C; NMR δ 2.61 (s, 3 H, Me), 3.3–4.0 (m, 4 H, SCH_2CH_2S), 3.90 (s,

(7) Deformylation of a 3-formylindole using ethylene glycol has been described: Kametani, T.; Kigawa, Y.; Takahashi, K.; Nemoto, H.; Fukumoto, K. *Chem. Pharm. Bull.* **1978**, *26*, 1918–1922.

3 H, OMe), 5.35 (s, 2 H, CH_2Ph), 6.32 [s, 1 H, $CH(S_2)$], 7.3-7.5 (m, 5 H, CH_2Ph), 9.58 (br s, 1 H, NH); MS, *m/e* 376 (39), 344 (100), 316 (80), 253 (88), 208 (28), 178 (30), 91 (100). Anal. Calcd for $C_{15}H_{15}NO_4$: C, 57.27; H, 5.07; N, 3.71. Found: C, 56.98; H, 5.05; N, 3.57.

Benzyl 3-Methyl-4-oxocyclopenta[*b*]pyrrole-2-carboxylate (23). A solution of sodium nitrite (1.5 g) in water (5 mL) was slowly added to a well-stirred solution of benzyl acetoacetate (4 g) in acetic acid (6 mL) while the temperature was kept below 10 °C. After standing in the refrigerator for 2 h, the solution was added slowly to a solution of 1,3-cyclopentanedione (Aldrich) (2 g) in acetic acid (4 mL). Simultaneously, a mixture of zinc dust (3.7 g) and anhydrous sodium acetate (3.7 g) was added, and after addition was complete the mixture was refluxed for 1 h and then poured onto ice water. The solid precipitate was filtered off and then chromatographed on thick-layer silica plates (elution with 30% ethyl acetate in hexane). The product was recovered from the silica with 50% ethyl acetate in hexane and gave 546 mg (10 %), mp 182-182.5 °C, after recrystallization from methanol: NMR δ 2.50 (s, 3 H, Me), 2.88 (s, 4 H, CH_2CH_2), 5.34 (s, 2 H, CH_2Ph), 7.40 (s, 5 H, Ph), 9.32 (br s, 1 H, NH); MS, *m/e* 269 (92), 178 (38), 161 (83), 135 (70), 108 (30), 91 (100). Anal. Calcd for $C_{16}H_{15}NO_3$: C, 71.36; H, 5.61; N, 5.20. Found: C, 71.32; H, 5.74; N, 5.40.

Benzyl 2-Acetyl-3,4-dimethylpyrrole-5-carboxylate (12). Benzyl 3,4-dimethylpyrrole-2-carboxylate[8] (1.03 g) was added to a solution of acetyl chloride (0.47 mL) in dichloromethane (10 mL) at 0 °C (ice bath); next, stannic chloride (0.77 mL) was added and the mixture was stirred and heated under reflux for 10 min. Analytical TLC indicated all starting material to be consumed at this stage, so the mixture was poured carefully into water, extracted with dichloromethane (50 mL), and dried (anhydrous Na_2SO_4). Evaporation to dryness gave a residue, which was chromatographed on alumina (Brockmann Grade III, elution with dichloromethane), and the appropriate eluates were evaporated to give a solid, which was crystallized from dichloromethane/ether to give white crystals (231 mg; 20%) with mp 103 °C: NMR δ, 2.28, 2.47 (each s, 6 H, 3 H, Me), 5.32 (s, 2 H, CH_2Ph), 7.40 (s, 5 H, Ph), 9.52 (br s, 1 H, NH). Anal. Calcd for $C_{16}H_{17}NO_3$: C, 70.83; H, 6.32; N, 5.16. Found: C, 70.55; H, 6.29; N, 5.16.

Ketal 13 from Benzyl 2-Acetyl-3,4-dimethylpyrrole-5-carboxylate (12): mp 93-94 °C; NMR δ 1.67, 2.04, 2.28 (each s, 3 H, Me), 3.91 (m, 4 H, OCH_2CH_2O), 5.32 (s, 2 H, CH_2Ph), 7.40 (m, 5 H, Ph), 8.93 (br s, 1 H, NH). Anal. Calcd for $C_{18}H_{21}NO_4$: C, 68.55; H, 6.71; N, 4.44. Found: C, 68.48; H, 6.65; N, 4.42.

Acetal 17 from Benzyl 2-Formyl-3-[2-(methoxycarbonyl)ethyl]-4-methylpyrrole-5-carboxylate (14): isolated as an oil; NMR δ 2.24 (s, 3 H, Me), 2.3-2.9 (m, 4 H, CH_2CH_2CO), 3.63 (s, 3 H, OMe), 3.8-4.0 (m, 4 H, OCH_2CH_2O), 5.25 (s, 2 H, CH_2Ph), 5.84 [s, 1 H, $CH(O_2)$], 7.30 (s, 5 H, Ph), 9.10 (br s, 1 H, NH).

Acetal 18 from Benzyl 3-Ethyl-2-formyl-4-methylpyrrole-5-carboxylate (15): isolated as an oil; NMR δ 1.02 (t, 3 H, CH_2CH_3), 2.21 (s, 3 H, Me), 2.24 (q, 2 H, CH_2CH_3), 3.9-4.1 (m, 4 H, OCH_2CH_2O), 5.28 (s, 2 H, CH_2Ph), 6.82 [s, 1 H, $CH(O_2)$], 7.34 (s, 5 H, Ph), 8.90 (br s, 1 H, NH).

Acetal 19 from Benzyl 2-Formyl-3-(methoxycarbonyl)-4-methylpyrrole-5-carboxylate (16): isolated as an oil; NMR δ 2.61 (s, 3 H, Me), 3.84 (s, 3 H, OMe), 4.0-4.2 (m, 4 H, OCH_2CH_2O), 5.35 (s, 2 H, CH_2Ph), 6.33 [s, 1 H, $CH(O_2)$], 7.41 (s, 5 H, Ph), 9.80 (br s, 1 H, NH).

Benzyl 2-[2-((3-Hydroxy-2,2-dimethylpropoxy)carbonyl)ethyl]-4-methylpyrrole-5-carboxylate (24): mp 88-89 °C; 12% yield, NMR δ 0.89 (s, 6 H, $C(Me)_2$), 2.30 (s, 3 H, Me), 2.66, 2.88 (each t, 2 H, CH_2CH_2CO), 3.28 (d, 2 H, CH_2OH), 3.94 (s, 2 H, CO_2CH_2), 5.32 (s, 2 H, CH_2Ph), 5.83 (d, J = 3 Hz, 1 H, 3-H), 7.3-7.5 (m, 5 H, Ph), 9.14 (br s, 1 H, NH). Anal. Calcd for $C_{21}H_{27}NO_5$: C, 67.54; H, 7.27; N, 3.75. Found: C, 67.69; N, 7.32; N, 4.06.

Acknowledgment. This research was supported by grants from the National Institutes of Health (HL 22252) and the National Science Foundation (CHE-81-20891). We are also grateful to Yarmouk University (Jordan) for financial support (to H.D.T.) and we thank Dr. K. C. Langry for preliminary experiments.

Registry No. 1, 2386-27-8; 2, 87462-14-4; 3, 2199-64-6; 4, 52459-21-9; 5, 40236-19-9; 6, 87462-15-5; 7, 2199-44-2; 8, 87462-16-6; 10, 6122-77-6; 11, 53700-88-2; 12, 53700-94-0; 13, 87462-17-7; 14, 16258-78-9; 15, 965-20-8; 16, 52459-21-9; 17, 87462-18-8; 18, 87462-19-9; 19, 87462-20-2; 23, 87462-21-3; 24, 87462-22-4; benzyl 3,4-dimethylpyrrole-2-carboxylate, 954-92-7; benzyl acetoacetate, 5396-89-4; 1,3-cyclopentanedione, 3859-41-4; acetyl chloride, 75-36-5.

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A Facile and Selective Methylation of 5-En-3-yn-1-ols with Titanium Tetrachloride-Trimethylaluminum Yielding (3*Z*)-4-Methylalka-3,5-dien-1-ols

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There is current interest in the nonrepetitive carbometalation of unsaturated carbon-carbon bonds using Ziegler-type titanium- or zirconium-organoalane reagents.[1-7] Negishi and co-workers[2] have had noteworthy success with Cp_2ZrCl_2-$AlMe_3$ in the selective methylmetalation of terminal alkynes. Methylmetal addition occurs in a syn fashion with the methyl group adding to the internal carbon. A variety of functionalized products can be derived from the carbometalated intermediates. Related to our interests is the further reaction of the zircomethylated products with ethylene oxide, leading to the isolation of (*E*)-4-methyl-3-alken-1-ols;[8] we have developed the complementary synthesis of (*Z*)-4-methyl-3-alken-1-ols by reaction of homopropargyl alcohols with $TiCl_4$-$AlMe_3$.[1]

In this paper we report a method to prepare (3*Z*)-4-methylalka-3,5-dien-1-ols (I) via the selective carbometalation of the yne group in 5-en-3-yn-1-ols with $TiCl_4$-$AlMe_3$. Our synthesis of I along with the Cp_2ZrCl_2-$AlMe_3$ routes to the 3*E* isomers (from 1-en-3-ynes and ethylene oxide) and (3*Z*)-3-methylalka-3,5-dien-1-ol (from 5-en-3-yn-1-ols) provide compounds that can be used as intermediates in the synthesis of sinensals, which have applications as orange flavorants.[9]

Experimental Section

Materials. 5-Methylhex-5-en-3-yn-1-ol and 7-methyloct-7-en-5-yn-3-ol were purchased from Farchan. The enynols have a tendency to polymerize and, therefore, were distilled under

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